Patients with end-stage renal disease receiving hemodialysis have a high risk of ischemic stroke. Potential explanations include prevalence of traditional vascular risk factors in this population, malnutrition, and possibly even hemodialysis itself attributable to volume shifts and blood pressure lability, although other unidentified factors may also play a role. A large prospective study of stroke in hemodialysis patients reported that cardioembolism was the most common stroke cause, although specific mechanisms were not reported. Patients on hemodialysis may be at greater risk to develop atrial fibrillation, presumed attributable to electrolyte shifts and structural cardiac changes. The incidence of bacteremia is also elevated in patients receiving hemodialysis, increasing the risk for infective endocarditis. In addition, venous thrombi are common in hemodialysis patients which may lead to paradoxical embolization in patients with a patent foramen ovale (PFO). We undertook this study to better characterize stroke causes among patients receiving hemodialysis and to specifically evaluate cardioembolic mechanisms.

Methods

We performed a retrospective chart review of hemodialysis patients admitted with an acute ischemic stroke to 2 hospitals in the University of Pennsylvania Health System: the Hospital of University of Pennsylvania and Penn Presbyterian Hospital. Both hospitals are located in West Philadelphia and together admit ≈700 patients with acute ischemic stroke annually. This project was approved by the institutional review board at the University of Pennsylvania. Using billing data collected between 2003 and 2010, we cross-referenced all inpatients with a diagnosis of stroke (discharge International Classification of Diseases, Ninth Revision, code between 430 and 436.99 or diagnosis related groups 14–17) with a list of hospital service charges for hemodialysis. Identified patients' charts were reviewed to confirm acute ischemic stroke, that hemodialysis was ongoing before the stroke event, and also to extract demographic and clinical data. The available diagnostic stroke evaluation was reviewed including neuroimaging (head computed tomography or magnetic resonance imaging), vascular studies (carotid and transcranial Doppler ultrasound, magnetic resonance angiography, computed tomography angiography, or conventional angiogram), and echocardiographic studies (transesophageal or transesophageal). Stroke cause was categorized by 2 independent raters using modified Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria. Stroke causes were categorized as large vessel, cardioembolic, small vessel, atypical, multiple causes, or cryptogenic. Discordant ratings were resolved by consensus. Comparisons were made using chi-squared, Fisher exact, and t tests as appropriate. Prevalence estimates and 95% confidence intervals for PFO were determined.
Results
The search query between 2003 and 2010 identified 171 patients, of which 52 patients were confirmed to have been receiving hemodialysis before hospitalization with acute stroke. Mean (±SD) age was 64±13 years, 29 (56%) were female, and 35 (67%) were black, 6 (12%) white, and 11 (21%) of unknown race. A history of hypertension was noted in 46 (88%), whereas 29 (56%) had a history of diabetes mellitus. Hemodialysis access included 9 (17%) with an arteriovenous graft, 23 (44%) with a tunneled catheter, and 20 (38%) with an arteriovenous fistula. Figure 1 displays the final determined stroke subtypes in this cohort. Cardioembolic mechanisms followed by cryptogenic mechanisms were most common. Among the 4 patients with multiple possible stroke mechanisms, all carried a diagnosis of atrial fibrillation. Figure 2 displays a Venn diagram of identified cardioembolic stroke mechanisms including 6 with acute infective endocarditis, accounting for 12% of the overall cohort. Excluding patients who were transferred to the University of Pennsylvania Health System, endocarditis accounted for 3 of 37 (8%) strokes. Overall, there were no statistical differences in demographic or vascular risk factors comparing patients with endocarditis to those without: age, 57 versus 65 years (P=0.14); hypertension, 100% versus 87% (P=1.00); and diabetes mellitus 67% versus 54% (P=0.68). There was also no association between endocarditis and type of hemodialysis access; endocarditis was seen in 3 of 21 (14%) patients with a fistula, 3 of 23 (13%) patients with a tunneled catheter, and 0 of 8 (0%) with a graft, P=0.72.

Transesophageal echocardiography only was performed in 36 patients (69%), and 16 (31%) received transesophageal echocardiography. Overall, PFO was identified in 5 of 52 patients (10%; 95% confidence interval, 1%–18%). Agitated saline contrast (bubble study) was performed in only 21 of 52 patients (40%), and PFO was identified in 3 of 21 patients (14%; 95% confidence interval, 0%–17%).

Discussion
This cohort of hemodialysis patients with stroke reveals that cardioembolic and cryptogenic stroke subtypes were most common. Among the 4 patients with multiple possible stroke mechanisms, all carried a diagnosis of atrial fibrillation. Figure 2 displays a Venn diagram of identified cardioembolic stroke mechanisms including 6 with acute infective endocarditis, accounting for 12% of the overall cohort. Excluding patients who were transferred to the University of Pennsylvania Health System, endocarditis accounted for 3 of 37 (8%) strokes. Overall, there were no statistical differences in demographic or vascular risk factors comparing patients with endocarditis to those without: age, 57 versus 65 years (P=0.14); hypertension, 100% versus 87% (P=1.00); and diabetes mellitus 67% versus 54% (P=0.68). There was also no association between endocarditis and type of hemodialysis access; endocarditis was seen in 3 of 21 (14%) patients with a fistula, 3 of 23 (13%) patients with a tunneled catheter, and 0 of 8 (0%) with a graft, P=0.72.

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Figure 1. Stroke causes in this cohort of hemodialysis patients.

Figure 2. Specific cardioembolic stroke mechanisms. *Other cardioembolic sources are chronic calcified endocarditis, thrombus on triple lumen catheter in right atrium with patent foramen ovale, and chronic calcified mitral valve thrombus.

were not provided in that study. In our cohort, we found an excess of infective endocarditis, much greater than has been reported in other stroke cohorts. Among a series of 402 consecutive patients with cardioembolic stroke, only 2 cases of endocarditis were reported. On the contrary, in patients with endocarditis, hemodialysis was a prevalent comorbidity. In a large prospective North American cohort of 597 cases of endocarditis, 21% were receiving hemodialysis. In looking for predictors of endocarditis, we found no clear association between type of hemodialysis access and endocarditis, likely related to limited power. In a series of 111 hemodialysis patients with Staphylococcus aureus endocarditis, 60% of patients had an indwelling catheter suggesting that this may be the highest risk.

We hypothesized that PFO would be prevalent among hemodialysis patients with stroke because PFO provides a right-to-left interatrial shunt and hemodialysis patients are at high risk for venous and right atrial thrombi. Despite this presumed risk for paradoxical embolization, the prevalence of PFO in this cohort was comparable with what has been described in population-based cohorts without stroke. There are important limitations to this study. As a retrospective case series, it is possible that there was systematic bias in patient acquisition. For example, critically ill patients with large strokes may not have continued hemodialysis if care was withdrawn or patients with mild stroke or transient ischemic attack may not have been hospitalized or not hospitalized long enough to require hemodialysis treatment. Finally, stroke evaluations were not systematic and many patients did not undergo a bubble study, the most sensitive means to identify a PFO, and thus we may have underestimated the prevalence of PFO in this cohort.

To conclude, this study of hemodialysis patients with acute stroke demonstrated that cardioembolic causes are the most common. Endocarditis was much more prevalent than in unselected stroke cohorts. Thus, a heightened index of suspicion for endocarditis is warranted in the hemodialysis population.

Disclosures
None.
References


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